PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing *(day/month/year)*	**27 JULY 2005 (27.07.2005)**
Applicant's or agent's file reference PCA50317/HMY	**FOR FURTHER ACTION** See paragraph 2 below

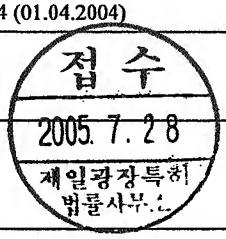
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/KR2005/000936	**31 MARCH 2005 (31.03.2005)**	01 APRIL 2004 (01.04.2004)

International Patent Classification (IPC) or both national classification and IPC

IPC7 A61K 9/52

Applicant

HANMI PHARM. CO., LTD. et al



1. This opinion contains indications relating to the following items:

- [x] Box No. I Basis of the opinion
- [ ] Box No. II Priority
- [ ] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV Lack of unity of invention
- [x] Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI Certain documents cited
- [ ] Box No. VII Certain defects in the international application
- [x] Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.
For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/KR	Authorized officer
Korean Intellectual Property Office 920 Dunsan-dong, Seo-gu, Daejeon 302-701, Republic of Korea	CHANG, Jin Ah
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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material
   - ☐ a sequence listing
   - ☐ table(s) related to the sequence listing

   b. format of material
   - ☐ in wirtten format
   - ☐ in computer readable form

   c. time of filing/furnishing
   - ☐ contained in the international application as filed.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additioanl copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims		YES
	Claims	1-5	NO
Inventive step (IS)	Claims		YES
	Claims	1-5	NO
Industrial applicability (IA)	Claims	1-5	YES
	Claims		NO

2. Citations and explanations :

1. Reference is made to the following documents:

D1= US 6340475 B2 (22 January 2002)

2. Novelty

The present invention claimed in claims 1-5 relates to a controlled release formulation of metformin or a pharmaceutically acceptable salt thereof comprising metformin or a pharmaceutically acceptable salt thereof as an active ingredient; a combination of a polyethylene oxide and a natural gum as a carrier for controlled release; and pharmaceutically acceptable additive.

D1 relates to extension of the duration of drug release within the stomach during the fed mode. In column 9 of D1, the combination of polyethylene oxide and zantan gum is disclosed as a combination of water-swellable polymer for a controlled drug release formulation, and in example 7, a controlled drug release formulation of metformin using polyethylene oxide having a molecular weight of 7,000,000 and zantan gum is disclosed.

(Continued on Supplemental Sheet.)

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The weight ratio of metformin to a controlled drug release carrier, 1:0.01 to 1: 1 of claim 5 is unclear. It is considered that it should be corrected to 1:0.01 to 1.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:

Box. V

Comparing the present invention with D1, both inventions are substantially the same in the objective of providing a controlled drug release formulation of metformin, the technical feature of the combination of water-swellable polymers such as a polyethylene oxide and a natural gum as a controlled release carrier, and the range of a molecular weight of polyethylene oxide. Thus, the subject matter of claims 1 to 5 does not meet the criteria for novelty set out in PCT Article 33(2).

3. Inventive Step

Concerning the effect of controlled drug releasing, there shows no improved effect in the result of the drug releasing experiments disclosed in figures 1-3, compared with that of the sustained release using polyethylene oxide and zantan gum described in figures 1,4,7 of D1.

Thus, the subject matter of claims 1 to 5 does not meet the criteria for an inventive step set out in PCT Article 33(3).

4.Industrial Applicability

The subject matter of claims 1-5 is considered to be industrially applicable under PCT Article 33(4).